UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/272,809	03/19/1999	JOHN CLARK LAGARIAS	23070-943	6118

7590 07/18/2002

LAW OFFICES OF JONATHAN ALAN QUINE
PO BOX 458
ALAMEDA, CA 94501

EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	22

DATE MAILED: 07/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/272,809	Applicant(s) LAGARIAS, JOHN CLARK	
	Examiner Ja-Na A Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sh et with the c rresp ndence address --

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1. The amendment filed 12 February 2002 has been entered. The examiner acknowledges the amendment to the specification. Claims 5-8 have been amended. Claims 1-32 are under consideration in this office action.

Claim Objections

2. Claims 5 and 8 are objected to because of the following informalities: Claim 5 refers to the "aopprotein" instead of an apoprotein. Claim 8 uses Cph2 however; it has not been previously defined. Appropriate correction is required.

Withdrawal of Rejections

3. The rejection of claims 1-3, 9-21 and 27-31 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 6-7, 9-11, 13-16, 19, 21-22 and 24-26 of U.S. Patent No. 6,046,014 is withdrawn.

New Grounds of Rejection
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a apoprotein

polypeptide consisting of the amino acids recited by SEQ ID NO: 9, does not reasonably provide enablement for a apoprotein polypeptide comprising between about 190 and about 400 amino acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The specification is not enabled for an apoprotein polypeptide comprising between about 190 and about 400 amino acids because the specification fails to teach polypeptides which such an identity; the specification lacks any description of a structure of a representative number of polypeptides encoding a representative number of polypeptides sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed; the specification fails to teach what the critical amino acid are and still achieve a the claimed polypeptide.

One of skill in the art would be reduced to merely randomly including or excluding amino acids which would lead to unpredictable results regarding the polypeptide. Absent factual evidence, the recite range of amino acids for the polypeptide is not deemed to reasonable support to one skilled in the art whether the claimed subject matter would be the same as that of such a similar known biomolecule.
In absence of further guidance from Applicants, the skilled artisan would have to discover what the appropriate amino acids would be. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use of the polypeptides. The inclusions and exclusions

of particular amino acids within the polypeptide would not predictably result in an enabled polypeptide. The specification does not provide guidance on how any amino acid can be included or excluded for the production of a polypeptide nor does the specification provide guidance on how any location can be used to produce a stable polypeptide. No working examples are shown containing the missing information. Thre are no examples of representative polypeptides, except for SEQ ID NO:9. Without such information, one of skill in the art could not predict which polypeptides would result in the desired polypeptide. Accordingly, one of skill in the art would be required to perform undue experimentation to use any amino acid to produce the claimed polypeptides. Therefore, one skilled in the art could not make and/or use the invention without undue experimentation.

5. Claims 1-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description Rejection.

The claims are drawn to a composition comprising an apoprotein polypeptide of between about 190 amino acids and about 400 amino acids and a method of detection the presence of a biomoleucle using an apoprotein of between 190 and 400 amino acids.

Polypeptides not having about 196 amino acids fail to meet the written description provision of 35 UCS 112, first paragraph. Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, make clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). The specification only discloses a polypeptide of about 196 amino acids, there is no disclosure of polypeptides having about 400 amino acid. Thus, the structure of the other polypeptides is not defined. The skilled artisan cannot envision the detailed structure of the encompassed by the polypeptides or what amino acid are. Therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method for determining sequence identity. Adequate written description requires more than a mere statement that it is part of the invention and a reference to a potential method of expression. The polypeptide and representative amino acid sequences are required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016.

The specification does not provide any polypeptides comprising an amino acid sequence of about 400 amino acids. There is no teaching of which amino acids may or may included without causing detrimental effects towards the production of the polypeptide. The specification fails to teach the structure of a representative number

polypeptides sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. Thus a skilled artisan cannot envision all the contemplated amino acid sequences by the detailed chemical structure of the claimed polypeptides and therefore conception cannot be achieved until reduction to practice has occurred. Furthermore, *In The Reagents of the University of California v. Eli Lilly*, (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of nucleic acids does not provide an adequate written description of the genus. Applicants are not required to disclose every species encompassed by a genus, thus the description of a genus is achieved by the recitation of a representative number of SEQ ID NO's, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a nucleic acid molecule...'requires a precise definition, such as by structure, formula, chemical name, or physical properties'".

The claims fail to recite the precise definition of the polypeptide amino acid sequences of about less then 400 amino acids. Currently the generic recitation of about 190 amino acids to about 400 amino acids is insufficient to support the claims as provided by the Interim Written Description Guidelines published in the June 15, 1998. In view of the lack of written description of the claims for failing to recite the precise definition of the polypeptides, the full breadth of the claims fail to meet the written description provision of 35 USC 112, first paragraph.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1-3, 6-7, 9-22, 25 and 27-32 are rejected under 35 U.S.C. 102(b) as being anticipated by Lagarias et al., WO 98/05944. Lagarias et al., teach a new class of fluorescent proteins that are useable as fluorescent markers (page 3 lines 24-26). The protein component comprises an apoprotein component and a nitrogen heterocyclic component that can be a tetrapyrrole or the particularly preferred phycoerythrobilin (page 4 lines 5-10). The apoprotein can be derived plants, green alga, or cyanobacteria or can be chemically synthesized (page 3 lines 12-15). Figure 10 illustrates a phytochrome operon of *Synechocystis* species. Truncated apoproteins consisting of a chromophore domain and the apoprotein N-terminal subsequence sufficient for lyase activity are preferred wherein the N-terminal sequence is less then about 400 amino acids (page 4 lines 30-24). The chromophore domain refers to the apoprotein N-terminal subsequence sufficient for lyase activity (page 7 lines 11-18). This domain of subsequences consist of preferable less than about 400 amino acids or even 390 or 350 amino acids (page 7 line 16). The fluorescent adduct can be covalently or noncovalenty linked to the label moiety (page 4 lines 25-27). The moiety can be any composition such as a biomolecule, including proteins, carbohydrates, lipids, members of a binding pair and nucleic acids (pages 4-5 lines 28-3). This invention also provides methods of use for the fluorescent adducts (page 5 lines 5-13). The method tests for the presence of a biomolecule in a sample comprising a biomolecule linked to a

fluorescent adduct consisting of an apoprotein and a bilin chromophore and contacting the sample with light which causes the fluorescent adduct to emit light and detect the emitted light thereby detecting the presence of the biomolecule (page 5 lines 13-24). The sample is contacted with light having a wavelength of about 570nm or about 590nm thereby allowing detection of the biomoleucle (page 5 lines 20-24).
Thus, Lagarias et al., WO 98/05944 teach a composition comprising an apoprotein polypeptide of between about 190 amino acids and 400 amino acids which comprises a lyase domain and a method of detecting the presence of a biomoleucle in a sample comprising the same steps as those recited in the instant application.

Response to Arguments

7. Applicant's arguments filed 12 February 2002 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

8. The rejection of claims 1-3, 6-7, 9-22, 25 and 27-32 are rejected under 35 U.S.C. 102(e) as being anticipated by Lagarias et al., US Patent 6,046,014 is maintained.

Applicants argue that patient '6,046,014 herein referred to as '014 offers no teaching or suggestion to modify the apoprotein to a length ranging from about 190 to

about 400 amino acids. However, '014 clearly teach the preferred truncated apoproteins consisting of a chromophore domain or the apoprotein N-terminal subsequence sufficient for lyase activity, wherein the N-terminal domain of consist of preferably less than about 400 amino acids. '014 further states that the chromophore domain comprise about 400, 390 or even 350 amino acids of the N-terminal domains. Therefore, '014 teach a composition comprising an apoprotein polypeptide of between about 190 and 400 amino acids by teaching truncated apoproteins. Moreover, the claim language recites "comprising" which is interpreted as open language. In view of the open language, the claims encompasses larger polypeptides that comprise the about 190 to about 400 amino acid polypeptide. Thus, '014 teach such compositions as recited by the claims. '014 also teach a method of detecting the presence of biomolecules in a sample comprising the steps of providing a sample; contacting the sample and detecting the presence of the biomolecule reciting the same steps as recited in the instant application. Thus Lagarias et al., teach the composition and method as claimed.

Applicants argues that the claims of '014 are generic and fail to render obvious the presently claimed invention. However, the specification of Lagarias et al., teach a composition comprising a apoprotein polypeptide comprising between about 190 and 400 amino acids and a method to detect the presence of a biomolecule in a sample comprising a biomolecule linked to a fluorescent adduct consisting of an apoprotein and a bilin chromophore and contacting the sample with light which causes the fluorescent adduct to emit light and detect the emitted light thereby detecting the presence of the biomolecule wherein the sample is contacted with light having a wavelength of about 570nm or about 590nm thereby allowing the detection of the biomolecule. The

teachings of '014 are not limited to only the claims but rather to the entire scope of the entire specification. Therefore, '014 teach the instant composition and method.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines
July 15, 2002

MARK NAVARRO
PRIMARY EXAMINER